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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/796,113	03/10/2004	Myron Spector	1194-176	2494

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EXAMINER	
GUCKER, STEPHEN	

ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
05/01/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/796,113	SPECTOR ET AL.	
	Examiner	Art Unit	
	STEPHEN GUCKER	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,5-7,9-11,14-17, 19 and 22-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,5-7,9-11,14-17, 19 and 22-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/9/09 has been entered.

2. Applicant's arguments filed 4/19/09 have been persuasive and have obviated all the grounds of all rejections of record, and said rejections have been withdrawn in lieu of the new U.S.C. 103 rejections set forth in this Office Action.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim ends with the phrase "nerve growth stimulate" when -–nerve growth stimulant-– was intended.

5. Claims 2-3, 5-6, 9-11, 19, 14-16, 22-30, and 32-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chamberlain et al. (reference 19 of IDS filed 3/10/04, "Chamberlain") in view of Geistlich et al. (reference 5 of IDS filed 3/10/04, US 5,837,278, "'278 patent") and further in view of Geistlich et al. (reference 1 of IDS filed 3/10/04, US 6,221,109, "'109 patent").

Chamberlain teaches collagen tubes for nerve regeneration that can be filled with a type I collagen/chondroitin-6-sulfate material (collagen and a glycosaminoglycan copolymer known as collagen-GAG (CG) copolymer) that acts as a nerve growth stimulant, and said tube is 20mm long with an internal diameter of 1.5mm (abstract, pages 1394-1395, and Figure 1). The collagen fiber filling material is longitudinally oriented with respect to the tube (page 1395). Laminin can be a promoter of nerve regeneration inside the tube (page 1394). Chamberlain discloses methods of placing nerves inside the tubes for regeneration (abstract and pages 1395-1396). (Myron Spector is a co-author of the Chamberlain et al. reference, and is also a co-inventor of the instant Application). Chamberlain does not teach a tube formed from a single sheet of collagen prepared from peritoneal membrane that has an outer smooth barrier surface and a soft fibrous surface opposite the smooth barrier surface. The '278 patent discloses a single sheet of a resorbable sidewall material consisting essentially of a single layer collagen sheet material having a compact, smooth outer barrier surface so as to inhibit cell adhesion thereon and act as a barrier to prevent passage of cells there through, and this sheet material further has a fibrous inner surface opposite the smooth barrier surface (column 1, line 51 to column 2, line 6) derived from collagen membrane peritoneal tissue (column 2, lines 52-60). This single layer collagen sheet material is identified as Bio-Gide® by the instant specification (page 3, paragraphs 0017 and 0018), and is the same material disclosed in the '278 patent. Bio-Gide® inherently meets all the claim limitations of claims 2-3, 11, 14-15, 23-28, and 33. (Peter Geistlich is a co-inventor for the '278 patent and is a co-inventor of the

instant Application). The '278 patent does not disclose that Bio-Gide® is suitable for use with nerve tissue. The '109 patent (second Geistlich et al. reference) teaches that Bio-Gide® can be wrapped around the spinal cord and dura sheath in order to protect both from injury during spinal surgeries and also to protect the spinal area from ingrowth of connective tissue and undesired cells which might interfere with proper healing (column 1, lines 9-18 and column 1, line 54 to column 2, line 9. Also see Figures 1 and 3). It would have been obvious to one of ordinary skill in the art at the time of the invention to make and use the collagen tubes of Chamberlain with the Bio-Gide® of the prior art patents because while Chamberlain teaches that collagen tubes have multiple advantages over silicone tubes, "the required characteristics of a nerve guide remain to be fully delineated" (page 1401). While porous collagen tubes permit diffusion of nutrients and growth-promoting factors from the external environment to the injured nerves in order to promote nerve regeneration (an observation supported by two studies according to Chamberlain), if the tube is too porous, important wound-derived neurotrophic factors may be allowed to exit the injury site prematurely through the tube. Chamberlain reports that his own study has shown that the most favourable results were obtained with a non-porous collagen tube filled with a CG copolymer because said tube facilitated the retention of the endogenous neurotrophic factors in the nerve injury gap site while allowing for the infiltration of smaller molecular weight nutrients through the tube. Chamberlain concludes "additional experimentation with porous and non-porous collagen tubes that differ in permeability may be used to address this issue" (page 1402), which is an explicit direct suggestion by the primary reference to substitute the finite group of other known collagen tubes for the known and motivating purpose of improving the therapeutic results. A clear nexus thus forms between the '109 patent which teaches Bio-Gide® collagen membranes formed into a tube around nerve tissue (spinal cord) (Figure 1 of the '109 patent) with the smooth barrier face facing the exterior to protect the

surgical site from ingrowth of unwanted cells (column 3, lines 5-10) while the fibrous face opposite the smooth face faces inward, allowing cell growth thereon (column 2, lines 1-4 and Figure 3), and the Chamberlain reference which discloses that "in the tubulization method of treating nerve gaps, tubes can enhance regeneration by serving to (1) contain matrices that have been found to enhance the regenerative process, perhaps by providing a scaffold for 'contact guidance'...(2) prevent ingrowth of adjacent tissue into the gap, and thereby prevent fibrocollagenous scar formation in the gap" (pages 1399-1400). Both the '109 patent and Chamberlain share a nexus to combine Bio-Gide® with the nerve regeneration methods of Chamberlain because Bio-Gide® has an interior surface that allows cell growth thereon ('109 patent) which is very similar to providing a scaffold for 'contact guidance' (Chamberlain). Likewise, Bio-Gide® has an exterior surface preventing ingrowth of unwanted cells ('109 patent) which is exactly equivalent to preventing ingrowth of tissue that would form scars in the nerve gap and inhibit nerve regeneration (Chamberlain). The '278 patent makes the connection between Chamberlain's suggestion to try other collagen tube materials in order to make and use a better nerve regeneration tube with the Bio-Gide® of the '109 patent even stronger because the '278 patent reiterates the advantages of Bio-Gide® in relation to its desired property of excluding unwanted cells and simultaneously providing a fibrous surface that improves the ability of wanted cells to grow (see claims 1 and 18 of the '278 patent). Finally, the '278 patent also teaches the advantages of making and using Bio-Gide® with chondroitin sulfate (claim 11) and glycosaminoglycan (claims 9, 12, and 24), which is also disclosed by Chamberlain for improving his collagen tubes (pages 1395 and 1402). Given the combined teachings of the three references, it would have been *prima facie* obvious to substitute the collagen of the nerve regeneration tubes of Chamberlain with the Bio-Gide® collagen of the patents because of the known advantageous properties of the two different surfaces of Bio-Gide® in order to make and use an

improved collagen nerve regeneration tube as explicitly and directly suggested by Chamberlain. Finally, because all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention because the nexus between all the references makes the substitution of a known similar product (Bio-Gide® collagen for collagen type I) from a finite list of known collagens for a known similar purpose (nerve tissue healing) in order to produce a known similar result (improved tissue healing by improved interior cell growth while excluding unwanted exterior cells) with a reasonable expectation of success is also *prima facie* obvious. See *KSR Int'l Co. v. Teleflex Inc., 127 S. Ct. 1727 (U.S. 2007)*.

6. Claims 2-3, 5-6, 9-11, 19, 14-17, 22-30 and 32-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chamberlain, the '278 patent, and the '109 patent as applied to claims 2-3, 5-6, 9-11, 19, 14-16, 22-30, and 32-33 above, and further in view of Fearnot et al. (US 6,358,284, "Fearnot").

Chamberlain, the '278 patent, and the '109 patent do not teach a step of joining two opposite side edges of a collagen sheet material together to form a tube. Fearnot does teach a process for producing an implantable graft construct from a sheet of a highly purified form of an implantable tela submucosa collagen matrix (column 6, lines 45-65) formed in the shape of a tube having a seam extending longitudinally along the length of the graft wherein the seam has been sealed to resist movement of fluids from the lumen through the seam to the exterior of the tube (column 3, lines 32-38). The tubular prosthesis is envisioned for use with nervous tissue (column 2, lines 63-64). It would have been obvious to one of ordinary skill in the art at the time of the invention to make an implantable graft construct from

a sheet of Bio-Gide® in the shape of a tube having a seam extending longitudinally along the length of the graft wherein the seam has been sealed to resist movement of fluids from the lumen through the seam to the exterior of the tube because of the desire to prevent wound-derived neurotrophic factors from leaking out as suggested by Chamberlain (page 14020).

7. Claims 2-3, 5-7, 9-11, 19, 14-16, and 22-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chamberlain, the '278 patent, and the '109 patent as applied to claims 2-3, 5-6, 9-11, 14-16, 19, 22-30, and 32-33 above, and further in view of Humes (US 5,429,938, already of record).

Chamberlain, the '278 patent, and the '109 patent do not teach a mixture of Type I and Type IV collagen in a ratio of about 1:1 for supporting biological activity. Humes does teach the use of Type I and Type IV collagen in about 1:1 ratios to support biological activity (column 3, lines 65-66). It would have been obvious to one of ordinary skill in the art at the time of the invention to employ Humes' ratio of about 1:1 of Type I and Type IV collagen because the other references do not quantitatively teach specific ratios between Type I and Type IV collagen for the desired aim of supporting biological activity. Chamberlain provides additional motivation by teaching that collagen tubes have multiple advantages over silicone tubes, but that "the required characteristics of a nerve guide remain to be fully delineated" (page 1401). While porous collagen tubes permit diffusion of nutrients and growth-promoting factors from the external environment to the injured nerves in order to promote nerve regeneration (an observation supported by two studies according to Chamberlain), if the tube is too porous, important wound-derived neurotrophic factors may be allowed to exit the injury site prematurely through the tube. Chamberlain reports that his own study has shown that the most favourable results were obtained with a non-porous collagen tube filled with a CG copolymer because said tube facilitated

the retention of the endogenous neurotrophic factors in the nerve injury gap site while allowing for the infiltration of smaller molecular weight nutrients through the tube. Chamberlain concludes "additional experimentation with porous and non-porous collagen tubes that differ in permeability may be used to address this issue" (page 1402), which is a suggestion by the primary reference to try to optimize the ratio of Type I and Type IV collagen for the known and motivating purpose of improving the therapeutic results. The artisan would be motivated to look to the Humes reference to supply this missing information if said artisan was actually going to reduce to practice a combination of Type I and Type IV collagen because such information would be required during fabrication and use of the neural regeneration tube.

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Gucker whose telephone number is 571-272-0883. The examiner can normally be reached on Mondays through Fridays from 0930 to 1800.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/S. G./
Examiner, Art Unit 1649
Stephen Gucker
April 29, 2009

/Robert C. Hayes/
Primary Examiner, Art Unit 1649